

Claims

1. An automated biological reaction apparatus having a reagent support carousel with a plurality of reagent container supports thereon, homing and indexing means associated with the support carousel for identifying the position of each reagent container support with reference to a home position during the operation of the apparatus, and drive means engaging the carousel for rotating the carousel and positioning a preselected reagent container support in a reagent supply zone.
2. An automated biological reaction apparatus of Claim 1 wherein the reagent support carousel is rotatably mounted on a reagent carousel support and the homing and indexing means comprises a proximity detection means and an object detectably by the proximity detection means when the proximity detection means and said object are in close proximity, one of said object and said proximity detection means being mounted on the reagent support carousel, and the other of the object and said proximity detection means being mounted on the reagent carousel support in a position adjacent the path of the other.
3. An automated biological reaction apparatus of Claim 2 wherein said object is metallic and mounted on the reagent support carousel and the proximity detector is a metal proximity detector mounted on the reagent carousel support.
4. An automated biological reaction apparatus of Claim 1 wherein the reagent support carousel is rotatably mounted on a reagent carousel support, the reagent support carousel has a bar code zone, and the homing and indexing means comprises a bar code reader mounted on the reagent

carousel support in a position to read a bar code on a reagent bottle positioned in the bar code zone, whereby a bar code identifying the contents of a reagent container in the respective reagent container support can be read with reference to said home position by the bar code reader, and the reagent container containing said identified reagent can be automatically positioned in the reagent supply zone.

5. An automated biological reaction apparatus of Claim 1 including a reagent delivery actuator means positioned for engaging a reagent container positioned in the reagent delivery zone and initiating delivery of a predetermined volume of reagent from the reagent container.

6. An automated biological reaction apparatus of Claim 1 wherein the drive means comprises a stepper motor having a rotational mode for rotating the reagent carousel and a braking mode resisting rotation of the reagent carousel.

7. An automated biological reaction apparatus of Claim 1 wherein the reagent support carousel comprises a reagent support tray removably supported by a reagent tray support, the reagent support tray has indexing support feet on the underside thereof, the reagent tray support has receptors for the indexing support feet in the upper surface thereof, whereby the reagent support tray can be removed from the reagent tray support for reloading or refrigerated storage and can be replaced on the reagent support tray in the same indexed position.

8. A slide support for an automated biological reaction apparatus comprising a slide support plate having a distal end, a proximal end, and a slide support surface, the distal end having raised terminal and lateral distal

guide tabs with guide tab termini, the proximal end having first and second lateral guides with opposed surfaces for engaging the lateral edges of a slide, the distance between the slide support surface and the guide tab termini being 5 less than a microscope slide thickness.

9. A slide support of Claim 8 wherein the support plate comprises a distal support section at the distal end and a proximal support section at the proximal end, the proximal support section comprising an inflexible support 10 and a flexible arm with opposed lateral edges, and the distance between the slide engaging surfaces is less than a microscope slide width, whereby the slide engaging surfaces apply a positive pressure against the edges of a slide engaged therewith.

15 10. A slide support of Claim 9 wherein the distance between the slide engaging surfaces is from 20 to 24 mm.

11. A slide support of Claim 8 including a pivot support with a pivot axis, wherein the slide support plate is pivotally mounted on the pivot support for rotation 20 around the pivot axis from a horizontal position to a slide draining position.

12. A slide support of Claim 11 wherein the pivot axis is defined by a pivot rod and a pivot rod receptor in sliding engagement therewith, one of the pivot rod and the 25 pivot rod receptor being attached to or integral with the slide support and the other of the pivot rod and pivot rod receptor being attached to or integral with the pivot support.

13. A slide support of Claim 12 wherein the pivot 30 axis is defined by two pivot rods and pivot rod receptors.

14. A slide support of Claim 11 wherein the slide support surface slopes downward from the proximal end to the distal end, the plane of the slide support surface forming an angle with the pivot axis of from 0.3 to 1°.

5 15. A slide support of Claim 11 wherein the slide support includes a lateral tilt cam surface for engagement by a tilt actuator.

16. A slide support of Claim 11 including a rotational bias means for retaining the support surface in  
10 the substantially horizontal position when the tilt cam surface is not engaged by a tilt actuator.

17. A slide support of Claim 16 wherein the rotational bias means is a spring.

18. A slide support of Claim 11 wherein the pivot  
15 support has a pivot stop means positioned to abut a surface of the slide support for stopping pivotal rotation of the slide support when it has been pivoted to the slide draining position.

19. An automated biological reaction apparatus having  
20 a slide support carousel with a plurality of slide supports mounted thereon in a circular array, homing and indexing means associated with the slide support carousel for identifying when the slide carousel is in a home position during the operation of the apparatus, and drive means  
25 engaging the carousel for rotating the carousel and positioning a slide support in a reagent delivery zone.

20. An automated biological reaction apparatus of Claim 19 wherein the slide support carousel is rotatably mounted on a slide carousel support, and the homing and

indexing means comprises a proximity detection means and an object detectable by the proximity detection means when the proximity detection means and said object are in close proximity, one of said object and said proximity detection  
5 means being mounted on the slide support carousel, and the other of the object and said proximity detection means being mounted on the slide carousel support in a position adjacent the path of the other.

21. An automated biological reaction apparatus of  
10 Claim 20 wherein said object is metallic and mounted on the slide support carousel and the proximity detector is a metal proximity detector mounted on the slide carousel support.

22. An automated biological reaction apparatus of  
15 Claim 19 wherein the slide support carousel is rotatably mounted on a slide carousel support, the slide support carousel has a bar code zone, and the homing and indexing means comprises a bar code reader mounted on the slide carousel support in a position to read a bar code on a  
20 slide positioned in the bar code zone.

23. An automated biological reaction apparatus of  
Claim 19 wherein the drive means comprises a stepper motor having a rotational mode for rotating the reagent carousel and a braking mode resisting rotation of the reagent  
25 carousel.

24. An automated biological reaction apparatus having a slide support carousel with a plurality of slide supports mounted thereon in a circular array, and drive means engaging the carousel for rotating the carousel and  
30 positioning a preselected slide support in a reagent delivery zone, heating means positioned for heating air and

passing the heated air over the slide supports, said heating means comprising a wall means around the slide support carousel defining a heating chamber, air distribution manifold means having a plurality of heated 5 air outlet ports positioned above the slide supports for distributing heated air over the upper surfaces of the slide supports, and air heater means.

25. An automated biological reaction apparatus of Claim 24 wherein the air heater means comprises an air 10 supply chamber communicating with the air distribution manifold, start-up and operational heating means positioned in the path of air passing from the air supply chamber to the air distribution manifold, the start-up heating means comprising means for heating air until the heating chamber 15 has reached an operational temperature, and the operational heating means comprising means for heating air until the heating chamber has reached said operational temperature and for intermittently heating air thereafter to maintain the heating chamber at an operational temperature.

20 26. An automated biological reaction apparatus of Claim 25 wherein the air heater means includes a fan positioned to force air into the air distribution manifold through the air supply chamber, said fan including air temperature responsive means for increasing the rotational 25 speed of said fan when the air temperature entering the air distribution manifold falls below a desired operational temperature.

27. An automated biological reaction apparatus of Claim 25 including a temperature sensing means positioned 30 in the path of heated air entering the air distribution manifold for detecting the temperature of said heated air.

28. An automated biological reaction apparatus of Claim 27 wherein the temperature sensing means is a thermistor encased in a heat sensitivity reducing jacket.

29. An automated biological reaction apparatus having  
5 a slide support carousel with a plurality of slide supports mounted thereon in a circular array, drive means engaging the carousel for rotating the carousel and positioning a slide support in a reagent delivery zone, and a rinse station, a rinse solution application means positioned  
10 adjacent the rinse station, the rinse solution application means comprising at least one nozzle positioned for directing a stream of rinse liquid onto a rinse solution impact zone of a slide support.

30. An automated biological reaction apparatus of  
15 Claim 29 wherein each slide support has a distal end, a proximal end, and a slide support surface, the distal end having raised terminal and lateral distal guide tabs with guide tab termini, the proximal end having first and second lateral guides with opposed surfaces for engaging the  
20 lateral edges of a slide, the distance between the slide support surface and the guide tab termini being less than a microscope slide thickness.

31. An automated biological reaction apparatus of Claim 30 wherein the slide support has a distal support  
25 section at the distal end and a proximal support section at the proximal end, the proximal support section comprising an inflexible support and a flexible arm with opposed lateral edges, and the distance between the slide engaging surfaces is less than a microscope slide width, whereby the  
30 slide engaging surfaces apply a positive pressure against the edges of a slide engaged therewith.

32. An automated biological reaction apparatus of Claim 31 wherein the distance between the slide engaging surfaces is from 20 to 24 mm.

33. An automated biological reaction apparatus of Claim 29, including a slide pivot support with a pivot axis, and wherein the slide support plate is pivotally mounted on the pivot support for rotation around the pivot axis from a horizontal position to a slide draining position.

10 34. An automated biological reaction apparatus of Claim 33 wherein the slide support includes a lateral tilt cam surface for engagement by the tilt actuator, and the apparatus includes a tilt actuator means positioned to applying pressure against the tilt cam surface and causing 15 the slide support to move from a substantially horizontal position to a drain position.

35. An automated biological reaction apparatus of Claim 34 including a rotational bias means for retaining the slide support surface in the substantially horizontal 20 position when the tilt cam surface is not engaged by a tilt actuator.

36. An automated biological reaction apparatus of Claim 35 wherein the rotational bias means is a spring.

37. An automated biological reaction apparatus of 25 Claim 36 wherein the pivot support has a pivot stop means positioned to abut a surface of the slide support for stopping pivotal rotation of the slide support when it has been pivoted to the slide draining position.

38. An automated biological reaction apparatus having



a slide support carousel with a plurality of slide supports mounted thereon in a circular array, drive means engaging the carousel for rotating the carousel and positioning a slide support in a reagent delivery zone and a evaporation  
5 inhibiting liquid application station, evaporation inhibiting liquid application means positioned adjacent the application station, the evaporation inhibiting liquid application means comprising at least one nozzle positioned for directing a stream of evaporation inhibiting liquid  
10 onto a preselected evaporation inhibiting liquid impact zone of a slide support.

39. An automated biological reaction apparatus of Claim 38 wherein the evaporation inhibiting liquid application station is in the reagent delivery zone.

15 40. An automated biological reaction apparatus having a slide support carousel with a plurality of slide supports mounted thereon in a circular array, drive means engaging the carousel for rotating the carousel and positioning a slide support in a reagent delivery zone, and a reagent  
20 support carousel with a plurality of reagent container supports thereon, homing and indexing means associated with the support carousel for identifying the position of each reagent container support with reference to a home position during the operation of the apparatus, and drive means  
25 engaging the carousel for rotating the carousel and positioning a preselected reagent container support in a reagent supply zone.

41. An automated biological reaction apparatus of Claim 40 wherein the reagent support carousel is rotatably  
30 mounted on a reagent carousel support and the homing and indexing means comprises a proximity detection means and an object detectably by the proximity detection means when the

proximity detection means and said object are in close proximity, one of said object and said proximity detection means being mounted on the reagent support carousel, and the other of the object and said proximity detection means 5 being mounted on the reagent carousel support in a position adjacent the path of the other.

42. An automated biological reaction apparatus of Claim 41 wherein said object is metallic and mounted on the reagent support carousel and the proximity detector is a 10 metal proximity detector mounted on the reagent carousel support.

43. An automated biological reaction apparatus of Claim 40 wherein the reagent support carousel is rotatably mounted on a reagent carousel support, the reagent support 15 carousel has a bar code zone, and the homing and indexing means comprises a bar code reader mounted on the reagent carousel support in a position to read a bar code on a reagent bottle positioned in the bar code zone, whereby a bar code identifying the contents of a reagent container in 20 the respective reagent container support can be read with reference to said home position by the bar code reader, and the reagent container containing said identified reagent can be automatically positioned in the reagent supply zone.

44. An automated biological reaction apparatus of 25 Claim 40 comprising a reagent delivery actuator means positioned for engaging a reagent container positioned in the reagent delivery zone and initiating delivery of a predetermined volume of reagent from the reagent container to a preselected reagent impact zone of a slide support in 30 the reagent delivery zone.

45. An automated biological reaction apparatus having

a slide support carousel with a plurality of slide supports mounted thereon in a circular array, drive means engaging the carousel for rotating the carousel and positioning a slide support in a vortex agitation zone, a vortex  
5 agitation means positioned adjacent the vortex agitation zone and having a nozzle means for directing air at the vortex agitation zone.

46. An automated biological reaction apparatus of Claim 45 wherein the vortex agitation means comprises a  
10 nozzle means for applying at least one gas stream to an off-center area of the surface of liquid on a slide in the vortex agitation zone.

47. An automated biological reaction apparatus of Claim 46 wherein the vortex agitation means comprises a  
15 first nozzle means adjacent to the distal end of a slide support in the vortex agitation zone for directing a first gas stream to a first off-center area of the surface of the liquid on a slide in the vortex agitation zone, and a  
second nozzle means adjacent to the proximal end of a slide  
20 support in the vortex agitation zone for directing a second gas stream to a second off-center area of the surface of the liquid on a slide in the vortex agitation zone, the first and second gas streams being in opposite directions and the first and second off-center areas being on opposite  
25 sides of the center of the surface of a liquid on a slide in the vortex agitation zone.

48. A heated liquid supply comprising a container having a top opening and a cap means for closing the opening, a heating jacket on at least a portion of the  
30 outer surface of the liquid container, insulation means surrounding the outer surface of the liquid container and the heating jacket, a temperature sensing means, a liquid

input conduit and a liquid output conduit extending into the liquid container through the cap means, the liquid input conduit having an outlet adjacent the top of the liquid container and the liquid output conduit having an inlet adjacent the bottom of the liquid container, and a power supply means connected to the temperature sensing means for energizing the heating jacket when the temperature of liquid in the container is below a lower predetermined level and for de-energizing the heating jacket when the temperature of liquid in the container is above an upper predetermined level.

49. A heated liquid supply of Claim 48 including a safety thermostat connected to the heating jacket for terminating flow of power to the heating jacket if the temperature of the container exceeds a predetermined safety limit above the upper predetermined level.

50. An improved biochemical method with increased sample dehydration protection comprising applying a biochemical reagent to the surface of a solid biological sample on a planar support surface, the improvement comprising

- a) covering the sample with an aqueous surface layer by applying an aqueous solution to the planar support surface adjacent the biological sample;
- b) covering the aqueous surface layer with an evaporation inhibiting liquid layer by applying the evaporation inhibiting liquid to the planar support surface adjacent the biological sample in an amount sufficient to form a continuous layer of evaporation inhibiting liquid over the sample, the evaporation inhibiting liquid being

5 substantially water-insoluble, substantially water-immiscible and substantially non-viscous; having a specific gravity less than water, and a boiling point above 100°C; and being devoid of chemical characteristics which would significantly interfere with biochemical reactions carried out on the sample; and

10 c) and treating the biological sample with an aqueous reagent solution by applying the reagent solution to the planar support surface adjacent the biological sample, whereby the reagent solution flows to the biological sample under the evaporation inhibiting liquid layer.

51. An improved biochemical method Claim 50 wherein 15 the evaporation inhibiting liquid is a substantially saturated alkane or cycloalkane having from 8 to 18 carbon atoms.

52. An improved method for mixing a reagent solution layer on a sample mounted on a planar support surface 20 comprising stirring the reagent solution by applying at least one gas stream to an area of the reagent solution layer between the center of the reagent solution layer and the edge of the planar surface, the axis of the gas stream forming an acute angle with the planar support surface.

25 53. An improved method of Claim 52 wherein the reagent solution layer is covered by a layer of an evaporation inhibiting liquid, the evaporation inhibiting liquid being substantially water-insoluble, substantially water-immiscible and substantially non-viscous; having a 30 specific gravity less than water, and a boiling point above 100°C; and being devoid of chemical characteristics which

would significantly interfere with biochemical reactions carried out on the sample...

54. An improved method of Claim 52 for mixing a reagent solution layer on a sample comprising applying two 5 gas streams to areas of the reagent solution layer to areas between the center of the reagent solution area and the edge of the planar support surface, the first gas stream being directed against a first reagent solution area and the second gas stream being directed against a second 10 reagent solution area, the first and second gas streams being in opposite directions, and the first and second reagent solution areas being on opposite sides of the center of the reagent solution area.

55. An improved method of Claim 54 wherein the 15 reagent solution layer is covered by a layer of an evaporation inhibiting liquid, the evaporation inhibiting liquid being substantially water-insoluble, substantially water-immiscible, and substantially non-viscous; having a specific gravity less than water, and a boiling point above 20 100°C; and being devoid of chemical characteristics which would significantly interfere with biochemical reactions carried out on the sample.

56. An automated biological reaction apparatus comprising:

- 25           a rotatable slide support carousel;
- a plurality of slide supports mounted on the slide support carousel in a circular array;
- drive means engaging the carousel for rotating the carousel;

a reagent delivery means for applying a predetermined quantity of reagent to a slide positioned, by rotation of the carousel, in a reagent delivery zone;

5 an evaporation inhibiting liquid application means positioned at the reagent delivery zone, the evaporation inhibiting liquid application means comprising at least one nozzle positioned for directing a stream of evaporation inhibiting liquid  
10 onto a preselected evaporation inhibiting liquid impact zone of a slide positioned at the reagent delivery zone;

15 a vortex agitation means positioned at a vortex agitation zone adjacent to the reagent delivery zone and having a nozzle means for directing fluid at the vortex agitation zone of a slide positioned at the vortex agitation zone;

heating means positioned for heating and passing a heated fluid over the slide supports; and

20 a rinse solution application means positioned at a rinse zone adjacent to the reagent delivery zone, the rinse solution application means comprising at least one nozzle positioned for directing a stream of rinse liquid onto a rinse solution impact zone of a  
25 slide positioned at the rinse zone; and

draining means for draining rinse solution from a slide.

57. An automated biological reaction apparatus of Claim 56 wherein a reagent carousel for supporting reagent

bottles and for positioning a selected reagent bottle at the reagent delivery zone is rotatably mounted on the slide support carousel.

58. An automated biological reaction apparatus of Claim 57 wherein identification means are provided for identifying each reagent bottle support by the reagent carousel and for identifying each slide supported by the slide support carousel.

59. An automated biological reaction apparatus of Claim 56 wherein the slide support has a slide support platform at a proximal end of the slide support adjacent an outer circumference of the slide support carousel and a slide support post at a distal end of the slide support adjacent an inner circumference of the slide support carousel, the distal end also including raised lateral distal guide tabs with guide termini between which a slide is positioned, wherein the slide support platform has a guide edge and a slide clamping arrangement for clamping a slide to the slide support, and wherein the distal guide termini are lower than an upper surface of the slide.

60. An automated biological reaction apparatus of Claim 59 wherein the vortex agitation means are positioned adjacent the inner circumference of the slide support carousel.

61. An automated biological reaction apparatus of Claim 56 further including a bar code reader for reading bar code on slides positioned of the slide supports.

62. An automated biological reaction apparatus of Claim 61 further including a bar code cleaner for cleaning bar codes on the slides.



63. An automated biological reaction apparatus of Claim 56 wherein the drain means comprises a jet drain for directing a jet of fluid across an upper surface of a slide.

5 64. An automated biological reaction apparatus of Claim 56 wherein the rinse solution application means comprises a first rinsing means at a beginning of the rinse zone and a second rinsing means at an end of the rinse zone.

10 65. An automated biological reaction apparatus of Claim 64 wherein the first rinsing means includes nozzle means for depositing a layer of rinse liquid onto an upper surface of a slide positioned at the beginning of the rinse zone and the second rinsing means includes sweeping means  
15 for sweeping the layer of rinse liquid off of the slide when the slide reaches the end of the rinse zone.

66. An automated biological reaction apparatus of Claim 65 wherein the first rinsing means and the second rinsing means are spaced from one another so that a  
20 predetermined period of time transpires during the transport of the slide between the first and second rinsing means before the layer of rinse liquid is swept off of the slide.

67. An automated biological reaction apparatus of  
25 Claim 66 wherein the sweeping means of the second rinsing means comprises fluid pulsing means for forming pulsed streams of rinse liquid, alternately directed at one and then an other of longitudinal edges of the slides, to sweep the layer of rinse liquid off of the slide.

30 68. A method for rinsing a slide having a fragile

tissue sample positioned on an upper surface thereof, the method comprising the steps of:

depositing a layer of rinse liquid onto the upper surface of the slide to form a layer of rinse liquid which covers the tissue sample;

waiting a predetermined period of time; and

sweeping the layer of rinse liquid off of the slide using a fluid stream.

69. A method according to Claim 68 wherein the step of depositing a layer of rinse liquid comprises:

pulsing a stream of rinse liquid at an area of the slide upstream from the tissue sample so that the rinse liquid has a laminar flow upon contact with the tissue sample to prevent damage thereto; and

15 forming the layer of rinse liquid on the upper surface of the slide due to the meniscus effect of the rinse liquid at edges of the slide.

70. A method according to Claim 68 wherein the step of waiting a predetermined period of time is set by a time of transport of the slide.

71. A method according to Claim 68 wherein the sweeping step comprises:

pulsing a first stream of rinse liquid at an area of the slide upstream from the tissue sample and toward one longitudinal edge of the slide so that the rinse liquid has a laminar flow upon contact with the tissue sample to

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